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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 14538A-45-1P	FOR FURTHER ACTION	See Noufication of Transmitul of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/13379	International filing date *(day/month/year)* 15 May 2000 (15.05.2000)	Priority date *(day/month/year)* 14 May 1999 (14.05.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 21/04; C12N 1/04, 5/10, 15/00, 15/29, 15/82; A01H 1/00, 5/00 9/00, 11/00 and US Cl.: 435/419, 440, 468; 536/23.6; 800/278, 290, 295		
Applicant FRED HUTCHINSON CANCER RESEARCH CENTER		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 9 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28 November 2000 (28.11.2000)	06 September 2001 (06.09.2001)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Cynthia Collins Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/13379

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-32 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 33 and 34, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-2, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-10, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 4 and 10-16

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ____ are so unclea that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 4, 10-16

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

WRITTEN OPINION

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-3, 5-9	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-3, 5-9	NO
Industrial Applicability (IA)	Claims 1-3, 5-9	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Certain Documents Cited

1. Certain published documents (Rule 70.10)

Application No Patent No.	Publication Date *(day/month/year)*	Filing Date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
None	None	None	None

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*
None	None	None

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:

Claims 1-3 and 5-9 lack an inventive step under PCT Article 33(3) as being obvious over WANG et al. I (1998) and WANG et al II (1997) in view of STREPP et al.

WANG et al I teach the identification of a functional Arabidopsis cyclin-dependent kinase inhibitor gene, ICK1 (page 451 Figures 1 and 2a).

WANG et al. II further teaches the specific interaction of the Arabidopsis cyclin-dependent kinase inhibitor gene ICK1 with the Arabidopsis D-like cyclin CycD3 (page 505 Figure 5 and page 506 Figure 6).

WANG et al. I and II do not teach a method of producing a hyperplastic plant by functionally inactivating the expression of a D-like cyclin-dependent kinase inhibitor gene using a targeting construct that inactivates expression via homologous recombination. WANG et al. I and II also do not teach the plant D-like cyclin-dependent kinase inhibitor gene BRO, or a plant having a functionally inactivated D-like cyclin-dependent kinase inhibitor gene.

STREPP et al. teach a method for producing a variant plant by functionally inactivating the expression of a plant nuclear FtsZ homolog gene, Pp*ftsZ*, using a targeting construct that inactivates expression via homologous recombination (pages 4368-4369 *Materials and Methods*, page 4370 *Figure 2A*, page 4371 *Figure 3*, page 4372 *Figure 4*). Disruption of the Pp*ftsZ* gene, a homolog of the bacterial cell division gene *ftsZ*, resulted in impeded division of plastids in transgenic plants (page 4369, column 2, 2nd full paragraph).

It would have been obvious to one of ordinary skill in the art to use STREPP et al.'s method to produce a hyperplastic variant plant by substituting a plant D-like cyclin-dependent kinase inhibitor gene as taught by WANG et al. II for the FtsZ homolog gene taught by STREPP et al., especially given the success of STREPP et al. in impeding plastid division by disrupting the Pp*ftsZ* gene, and given the recognition by those of ordinary skill in the art that inactivation of a D-like cyclin-dependent kinase inhibitor gene would inactivate a negative regulator of cell division.

Claims 1-3 and 5-9 lack an inventive step under PCT Article 33(3) as being obvious over WANG et al. I and WANG et al II in view of VALANCIUS et al.

The teachings of WANG et al. I and II are discussed *supra*.

VALANCIUS et al. teach a method for making small insertional changes in a gene using a targeting construct that operates via homologous recombination (page 1403).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

It would have been obvious to one of ordinary skill in the art to use VALANCIUS et al.'s method to produce a hyperplastic variant plant by making small insertional changes in a plant D-like cyclin-dependent kinase inhibitor gene as taught by WANG et al. II, especially given the recognition by those of ordinary skill in the art that insertional inactivation of a D-like cyclin-dependent kinase inhibitor gene would inactivate a negative regulator of cell division.

---------- NEW CITATIONS ----------

STREPP et al. Plant nuclear gene knockout reveals a role in plastid division for the homolog of the bacterial cell division protein FtsZ, an ancestral tubulin. Proc. Natl. Acad. Sci. USA. April 1998, Vol. 95, pages 4368-4373, see pages 4368-4372.